

SEPTEMBER
23-27TH
2024



BRAZILIAN MEETING
ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

Synthesis of a new series of 1,2,3-triazole-4-yl-phosphonates

Gabriel Tavares de Almeida Pinto^{1*}, Maria Tereza Miranda Martins¹, Luiz Claudio Ferreira Pimentel²
Matheus Ouverney Ferreira and Anna Claudia Cunha¹

1) Department of Organic Chemistry, Fluminense Federal University, UFF, 24020-141

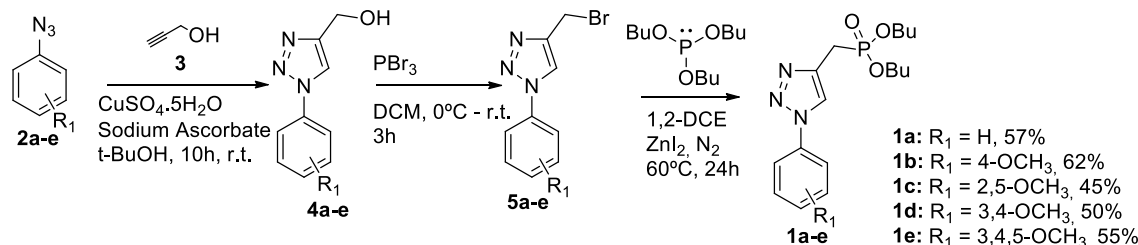
2) Department of Drug Synthesis, Farmanguinhos, Oswaldo Cruz Foundation, FIOCRUZ, 21040-360

*e-mail: gabrieltavares@id.uff.br

Keywords: 1,2,3-triazoles, phosphonates, click chemistry

ABSTRACT

Triazoles are known for their diverse biological activities and wide applicability in medicinal chemistry¹, materials science¹, and chemical synthesis². They often serve as pharmacophore groups due to their favorable chemical properties, which include hydrogen bonding capabilities, and potential for π - π stacking interactions with biological targets³. Similarly, the phosphonate group acts as a pharmacophore by providing key interactions that can enhance a drug's binding affinity, and overall efficacy⁴. The combination of these two functionalities in a single molecule – 1,2,3-triazole and phosphonate – opens up possibilities for the development of new pharmacologically active compounds. Future studies will focus on the detailed biological evaluation of the 1,2,3-triazole-4-yl-phosphonates **1a-e** (Scheme) in various disease models. The synthesis of **1a-e** initially involved the 1,3-dipolar cycloaddition reaction between azides **2a-e** and **3**, followed by bromination of **4a-e**. The nucleophilic substitution reaction to the saturated carbon of **5a-e** with tributyl phosphite provided the desired compounds **1a-e** in moderate yields.



Scheme. Preparation of phenyl-1,2,3-triazole phosphonates

ACKNOWLEDGEMENTS

CAPES, UFF, PPGQ-UFF, FAPERJ, PIBITI/CNPq.

REFERENCES

- 1- Morais, P. A. B.; Javarini, C. L.; Valim, T. C.; Francisco, C. S.; Ferreira, L. C. F.; Bottocim, R. R. T.; Neto, A. C.; Júnior, V. L. Triazole: A New Perspective in Medicinal Chemistry and Material Science. *Curr. Org. Chem.* **2022**, 26 (18), 1691–1702. DOI: 10.2174/1385272827666221213145147.
- 2- De Moraes, R. S. M.; Martins, M. T. M.; Pinto, G. T. A.; Rodrigues, S. C.; Nascimento, P. A.; Cruz, C. C.; Góes, K. D.; Cunha, A. C. An Overview on Generation and General Properties of N-Heterocyclic Carbenes: Applications of 1,2,4-Triazolium Carbenes as Metal Free Organocatalysts. *Arab. J. Chem.* **2024**, 17 (2), 105527. DOI: 10.1016/j.arabjc.2023.105527.
- 3- Guan, Q.; Xing, S.; Wang, L.; Zhu, J.; Guo, C.; Xu, C.; Zhao, Q.; Wu, Y.; Chen, Y.; Sun, H. Triazoles in Medicinal Chemistry: Physicochemical Properties, Bioisosterism, and Application. *J. Med. Chem.* **2024**. DOI: 10.1021/acs.jmedchem.4c00652.
- 4- Rodriguez, J. B.; Gallo-Rodriguez, C. The Role of the Phosphorus Atom in Drug Design. *ChemMedChem.* **2018**. DOI: 10.1002/cmdc.201800693.